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Synthesis of Heteroannulated Indolopyrazines through Domino N−H Palladium-Catalyzed/Metal-Free Oxidative C−H Bond Activation

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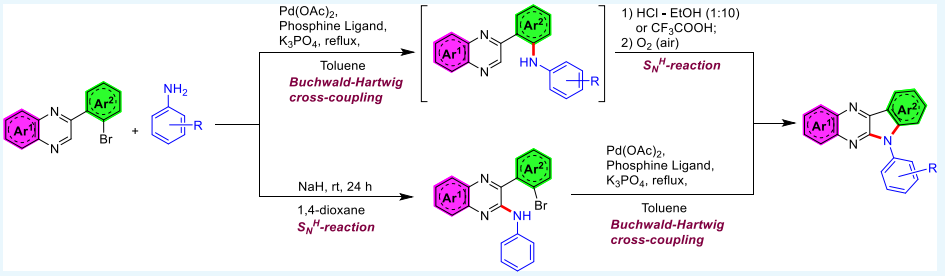

ABSTRACT: A convenient approach to [1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-*b*]indoles and their heteroannulated analogues bearing various aryl substituents in the backbone has been developed. This synthetic protocol is based on Pd-catalyzed Buchwald−Hartwig and subsequent annulation by intramolecular oxidative cyclodehydrogenation. The photophysical properties for new polycycles have been measured.

INTRODUCTION

Indolo[2,3-*b*]pyrazines are significant structural motifs possessing many important applications such as in medicinal chemistry and material sciences (Figure 1). Namely, indolo[2,3-*b*]pyrazine derivatives display a wide range of promising biological activities, such as antibacterial,[1] anticancer,[2] and antiviral activities.[3] Many indolopyrazine derivatives have also been suggested as promising materials for organic electronics such as organic light-emitting diodes,[4] solar cells,[5] and organic transistor memory devices.[6]

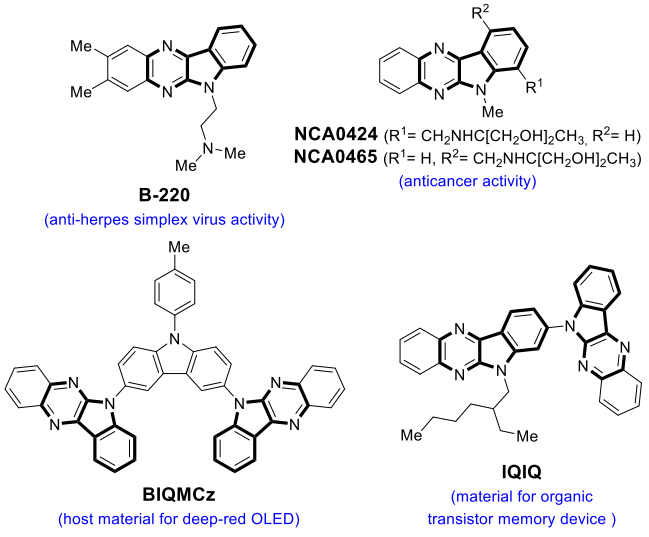

Figure 1. Representative compound bearing the indolo[2,3-*b*]-pyrazine core.

There are five main routes for construction of the indolopyrazine core that are described in the literature, and they should be discussed to identify their weaknesses (Scheme 1). The most famous methods for the preparation of indolopyrazine consist in the condensation of isatin with *o*-phenylenediamine (route 1, Scheme 1)[1,2c,6,7] or condensation of *in situ*-generated 2,3-diaminoindole with *α*-dicarbonyl compounds (route 2, Scheme 1).[8] Generally, the main limitations of these methods are obtaining regioisomeric mixtures of indolopyrazines, when unsymmetrical *o*-phenylenediamines or *α*-dicarbonyl compounds are used. Buchwald−Hartwig amination followed by C−H activation from secondary amines and 2,3-dibromoquinoxaline in one pot (route 3, Scheme 1)[9] and a two-step approach using Suzuki cross-coupling and subsequent annulation by Pd-catalyzed

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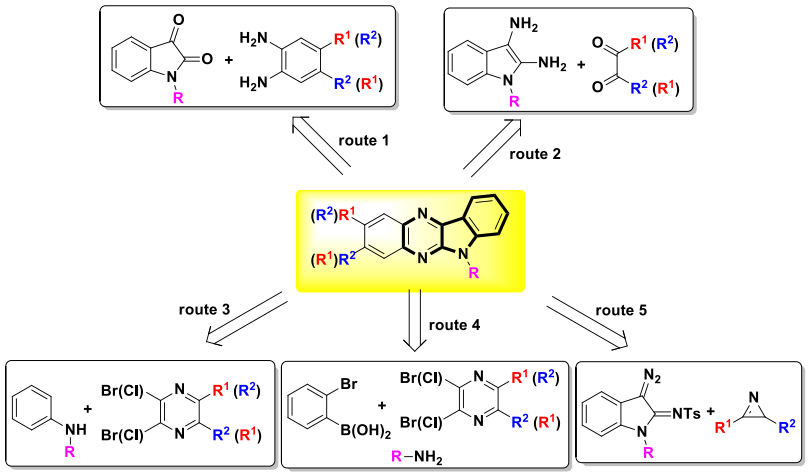
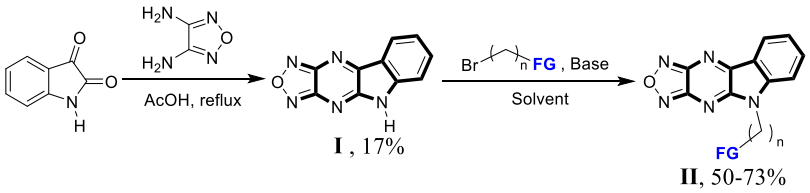
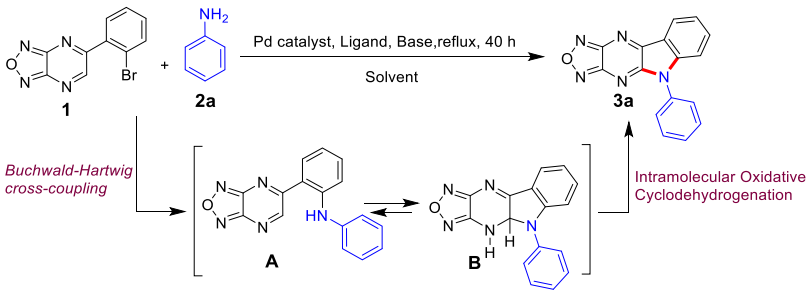
Scheme 1. Synthetic Routes to the Formation of the Indolo[2,3-*b*]pyrazine Scaffold



Scheme 2. Synthesis of 5*H*-[1,2,5]Oxadiazolo[3′,4′:5,6]pyrazino[2,3-*b*]indole (I) and its 5-Alkyl-Substituted Derivatives (II)



Scheme 3. Domino Synthesis of 5-Phenyl-5*H*-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-*b*]indole 3a



twofold C−N coupling reactions with primary amines (route 4, Scheme 1)[10] afford indolo[2,3-*b*]pyrazines in high yield but they similarly do not possess regioselectivity. Furthermore, routes 3 and 4 have not corresponded the concept of the pot, atom, and step economic (PASE)[11] synthetic procedure because it requires using 2,3-di(chloro)bromopyrazines that is necessary for an additional introduction of halogens in the pyrazine ring. Another regioselective method for the synthesis of the indolopyrazines based on a sequential rhodium-catalyzed formal [3+3] cycloaddition and aromatization reaction of various diazoindolinimines with azirines.[12] This protocol requires a highly expensive and non-eco-friendly rhodium catalyst and infrequent raw materials. All these features eventually lead to the necessity of developing new PASE processes to synthesize indolopyrazine and their heteroanalogues that will be based on the metal-free oxidative C−H bond functionalization (so-called S_N^H reaction).[13]

It should be mentioned that [1,2,5]oxadiazolo[3,4-*b*]-pyrazine (so-called " furazanopyrazine") exhibits higher electron-withdrawing character than similar nonannulated pyrazine analogues and can be readily involved into the metal-free oxidative C−H bond functionalization.[14] Nowadays, there is only one example of the synthesis of unsubstituted 5*H*-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-*b*]indole (**I**) and its 5-alkyl-substituted derivatives (**II**) as a new family of effective inhibitors for the *β*-catenin/T-cell factor protein−protein interaction (Scheme 2).[15]

By the foregoing, furazanopyrizine derivatives have been selected as major precursors of novel aryl-substituted 5*H*-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-*b*]indoles.

RESULTS AND DISCUSSION

Synthesis. It has been found that the reaction of 5-(2-bromophenyl)-[1,2,5]oxadiazolo[3,4-*b*]pyrazine **1** with aniline **2a** afforded 5-phenyl-5*H*-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino-[2,3-*b*]indole **3a** in good yield (Scheme 3). The conditions of the domino reaction of **1** with aniline **2a** were optimized (Table 1). The ligand, palladium precursor, base, and solvent were varied. The results showed that tricyclohexylphosphine (PCy_3) often gave better yields than other ligands. In fact, up to 45% yield of **3a** was achieved by employment of PCy_3 as a ligand in combination with $Pd(OAc)_2$ as the Pd source (Table 1, entry 10).

With the optimized conditions in hand, we examined the scope of the twofold C−N annulation reaction of **1** with

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Table 1. Optimization for the Synthesis of 3a

entry	Pd precursor (equiv)	ligand (20 mol %)	base (2.5 equiv)	solvent	yield 3a (%)
1	$Pd(PPh_3)_4$ (5 mol %)		K_3PO_4	1,4-dioxane	0
2	$Pd(PPh_3)_4$ (10 mol %)		K_3PO_4	1,4-dioxane	9
3	$Pd(PPh_3)_2Cl_2$ (10 mol %)	PPh_3	K_3PO_4	1,4-dioxane	15
4	$Pd_2(dba)_3$ (10 mol %)	PCy_3	K_3PO_4	1,4-dioxane	28
5	$Pd(OAc)_2$ (10 mol %)	XantPhos	K_3PO_4	1,4-dioxane	35
6	$Pd(OAc)_2$ (10 mol %)	XPhos	K_3PO_4	1,4-dioxane	33
7	$Pd(OAc)_2$ (10 mol %)	PCy_3	DABCO	1,4-dioxane	0
8	$Pd(OAc)_2$ (10 mol %)	PCy_3	K_2CO_3	1,4-dioxane	35
9	$Pd(OAc)_2$ (10 mol %)	PCy_3	K_3PO_4	1,4-dioxane	40
10	$Pd(OAc)_2$ (10 mol %)	PCy_3	K_3PO_4	toluene	45

various anilines **2b**−**i** and benzylamine **2j**. The results showed that the annulations gave the same yields for anilines bearing both electron-withdrawing and -donating substituents. However, the domino reactions with sterically crowded *ortho*-**2b**,**f** and *meta*-substituted **2c**,**g** anilines have resulted in the expected 5-aryl-5*H*-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-*b*]indole **3** in lower yields than with unsubstituted **2a** and para-substituted **2d**,**h** anilines (Scheme 4). In contrast, the reactions of **1** with alkylamines, using our optimized conditions (Table 1, entry 10), resulted in the formation of side products which were difficult to separate from the main product. The appropriate result was only achieved for the synthesis of product **3j** derived from benzylamine in 59% yield. Structures of 5*H*-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-*b*]indoles were verified by X-ray diffraction analysis performed for the single-crystal sample of 5-(*m*-tolyl)-substituted derivative **3i** (Figure 2), thus supporting the ^1H and ^{13}C NMR spectroscopic data.

A feasible reaction mechanism is depicted in Scheme 3. The reaction between the **1** and aniline **2a** proceeds through the Buchwald−Hartwig amination, which gives intermediate **A**, followed by an intramolecular nucleophilic attack at C(6)

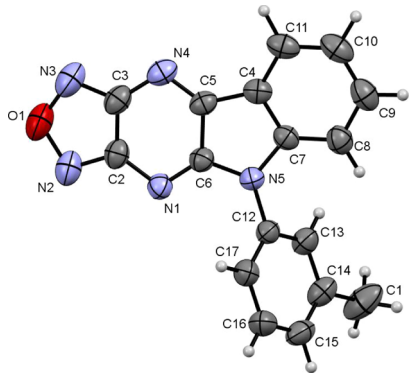


Figure 2. ORTEP of **3i** with thermal ellipsoids at the 50% probability level.

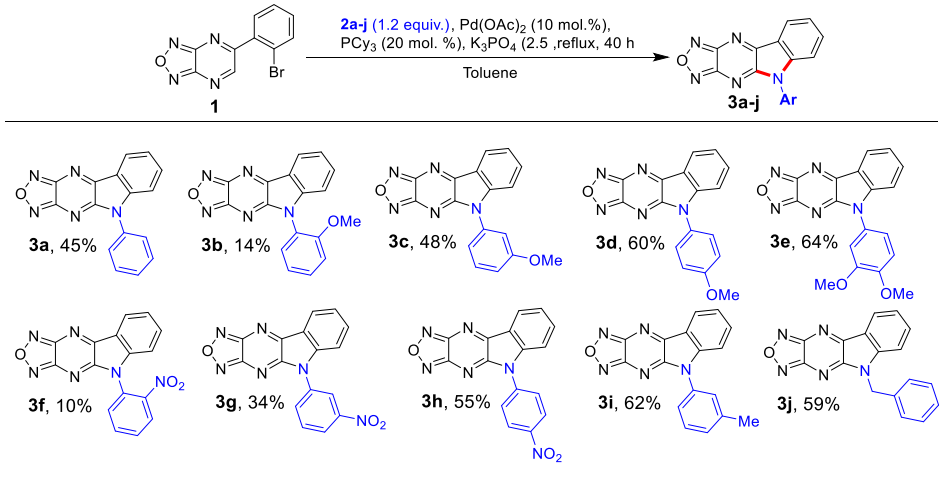
position furazanopyrizine core **B**. The subsequent oxidation of dihydropyrazine intermediate **B** by air oxygen leads to the polycyclic system **3a**.

To confirm this hypothesis, we carried out the reactions of furazanopyrazine **1** with aniline **2a** without using any palladium catalyst only in the presence of various bases. It has been shown that transition-metal-free oxidative dehydrogenation cross-coupling reaction leads to **4a** with the highest yield of 55% in the presence of sodium hydride as a base (Scheme 5). Using these conditions allowed us to obtain a wide range of corresponding S_N^H products by the reaction of **1** with the same series of amines. It is supposed that these reactions' C−H functionalization proceeds through nucleophilic substitution of hydrogen according to the two-step "Addition−Oxidation" mechanism.[13]

To increase the yields of polycyclic compounds **3**, we have carried out the annulation reaction of **4a** in the earlier developed best conditions of Buchwald−Hartwig amination (Scheme 6). Unfortunately, despite yields of intramolecular C−N coupling annulation being 72%, the two-step overall yield of **3a** from compound **1** to **3a** achieved only to 40%.

The suggested approach to the construction of the indolo[2,3-*b*]pyrazine core has also been applied successfully for the synthesis of different indolopyrazines with annulated benzene and/or thiophene rings (Scheme 7). In this regard, it is noteworthy that the only reaction of 5-(3-bromothiophen-2-yl)-[1,2,5]oxadiazolo[3,4-*b*]pyrazine **5a** with aniline **2a** yielded

Scheme 4. Synthesis and Structures of 5*H*-[1,2,5]Oxadiazolo[3′,4′:5,6]pyrazino[2,3-*b*]indole Derivatives 3a−j



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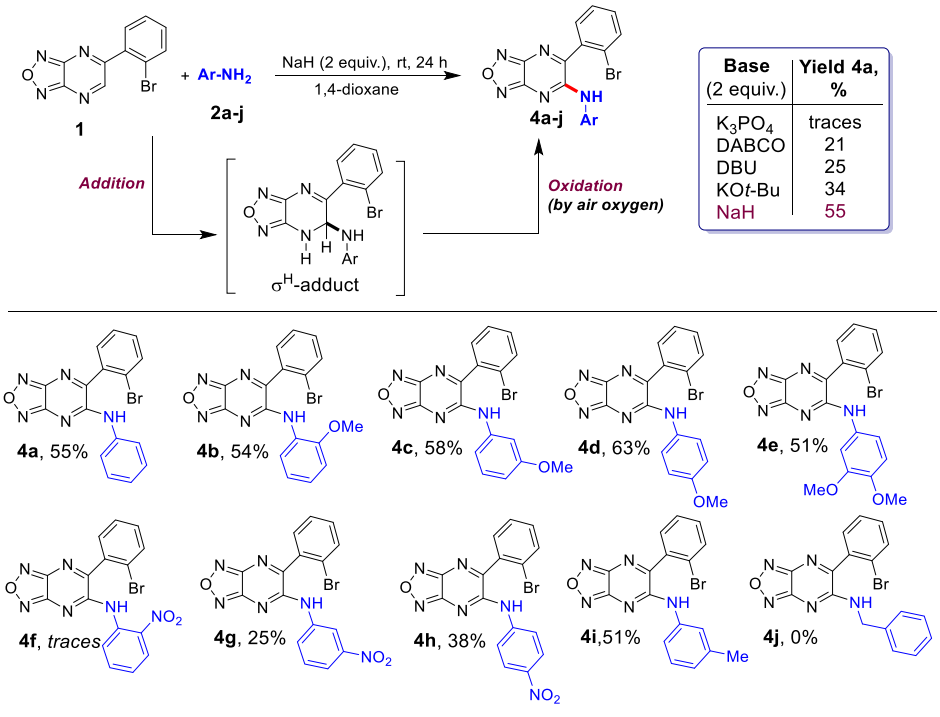
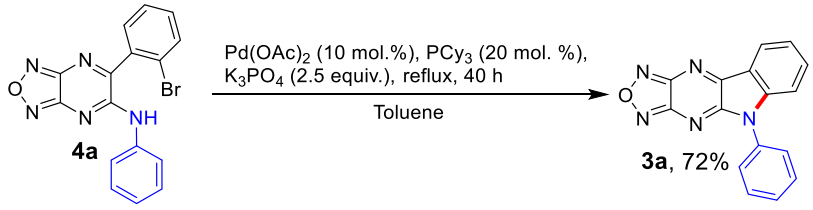
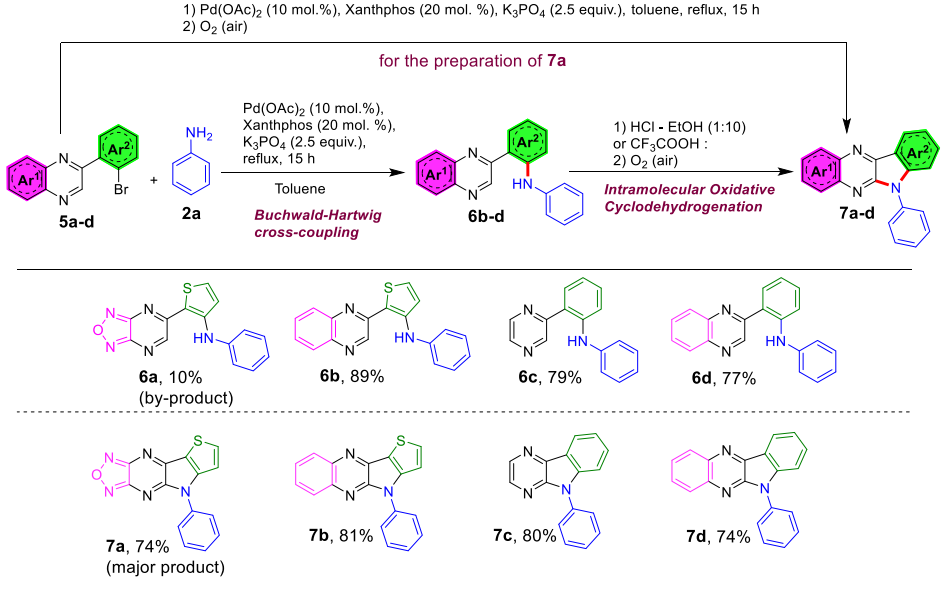
Scheme 5. Synthesis and Structures of *N*-Aryl-6-(2-bromophenyl)-[1,2,5]oxadiazolo[3,4-*b*]pyrazin-5-amines 4a−i



Scheme 6. Synthesis of 5-Phenyl-5*H*-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-*b*]indole 4a by Intramolecular Buchwald−Hartwig Amination



Scheme 7. Synthesis of Heteroannulated Indolopyrazine Derivatives 7a−d



desired 8-phenyl-8*H*-[1,2,5]oxadiazolo[3,4-*b*]thieno-[2′,3′:4,5]pyrrolo[2,3-*e*]pyrazine **7a** and compound **6a** as a by-product. In other cases, the reactions of the bromine-substituted derivatives **5b−d** with aniline **2a** led to the classic Buchwald−Hartwig amination products **6b−d** in 77−89% yields. Notably, using PCy_3 as a ligand for the palladium

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catalyst in this case afforded products in yields only up to 40%, while the replacement of it by Xantphos significantly increased the yield of compounds **6b−d**.

Further treatment of amination products **6b−d** by acids, followed by oxidation with air oxygen, also leads to similar cyclization products **7b−d**. Following the literature, trifluoroacetic acid[16] was used for the cyclization of thiophenyl-substituted quinoxaline **6b**, while a mixture of hydrochloric acid[17] in ethanol led to the transformation of amino derivatives **6a,c** into indolopyrazines **7c,b** in high yields (Scheme 7).

CONCLUSIONS

In summary, we have described a convenient approach to construct derivatives of a key heterocyclic system, namely, [1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-*b*]indoles, bearing various substituents in the pyrrole fragment, based on domino Pd-catalyzed Buchwald−Hartwig and subsequent annulation by intramolecular oxidative cyclodehydrogenation reactions. The two-step synthesis of other heteroannulated indolopyrazine analogues has been realized using this synthetic approach. The further design and synthesis of different indoloannulated derivatives using this reaction procedure, as well as the elucidation of photophysical and electronic properties of these polycyclic compounds, are currently in progress.

EXPERIMENTAL SECTION

General Information. All reagents and solvents were obtained from commercial sources and dried using standard procedures before use. ^{1}H and ^{13}C NMR spectra were obtained on Bruker DRX-400, AVANCE-500, and AVANCE-600 spectrometers with TMS as internal standards. Elemental analysis was carried out on a Eurovector EA 3000 automated analyzer. Melting points were determined on Boetius combined heating stages and were not corrected. All solvents used were dried and distilled as per standard procedures. IR spectra of samples (solid powders) were recorded on a Spectrum One Fourier transform IR spectrometer (PerkinElmer) equipped with a diffuse reflectance attachment (DRA). UV−vis spectra were recorded for ∼10^{-5} to 10^{-6} M CH_2Cl_2 solutions with a Shimadzu UV-2401PC spectrophotometer. X-ray diffraction analysis was performed on an automated X-ray diffractometer "Xcalibur E" based on the standard procedure. The deposition number CCDC 1989238 for **3i** contains the Supporting Information crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General Procedure for the Synthesis of 2-Bromophenyl and 3-(Bromothiophen-2-yl)-Substituted 1,4-Diazine Derivatives (1 and 5a−d). Selenium dioxide (1.1 g, 10 mmol) was dissolved in 1,4-dioxane/H_2O 15:1 (16 mL) and the mixture was heated at reflux for 5 min. 2′-Bromoacetophenone [or 2-acetyl-3-bromothiophene] (10 mmol) was added and heating continued for next 12 h. The reaction mixture was filtered and the filtrate was concentrated under reduced pressure to give the corresponding aryl glyoxal as light-yellow oil. The solution of 3,4-diaminofurazan [or 1,2-phenylenediamine] (10 mmol) and crude aryl glyoxal in a mixture of EtOH (5 mL) and CH_3COOH (5 mL) was refluxed for 1 h. After that, the mixture was cooled down, and the precipitate was filtered off and washed with ethanol and then air-dried.

*5-(2-Bromophenyl)-[1,2,5]oxadiazolo[3,4-b]pyrazine (**1**).* 2′-Bromoacetophenone and 3,4-diaminofurazan were used for the synthesis of product **1**.

Yellow powder; yield 2.19 g (79%); mp 135 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.44 (s, 1H), 7.91 (dd, J = 8.0, 1.1 Hz, 1H), 7.79 (dd, J = 7.6, 1.7 Hz, 1H), 7.68 (td, J = 7.6, 1.1 Hz, 1H), 7.63−7.59 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 162.4, 157.1, 151.9, 151.1, 136.1, 133.4, 133.1, 132.4, 128.5, 121.0. Anal. Calcd for $C_{10}H_5BrN_4O$ (277.08): C, 43.35; H, 1.87; N, 20.22. Found: C, 43.41; H, 1.84; N, 20.10.

*5-(3-Bromothiophen-2-yl)-[1,2,5]oxadiazolo[3,4-b]-pyrazine (**5a**).* 2-Acetyl-3-bromothiophene and 3,4-diaminofurazan were used for the synthesis of product **5a**.

Pale yellow powder; yield 2.15 g (76%); mp 174−176 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.79 (s, 1H), 8.19 (d, J = 5.3 Hz, 1H), 7.46 (d, J = 5.3 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 154.5, 154.0, 151.9, 151.1, 135.3, 134.2, 134.1, 114.8. Anal. Calcd for $C_8H_3BrN_4OS$ (283.10): C, 33.94; H, 1.07; N, 19.79. Found: C, 33.92; H, 0.96; Br, 28.22; N, 19.69.

*2-(3-Bromothiophen-2-yl)quinoxaline (**5b**).* 2-Acetyl-3-bromothiophene and 1,2-phenylenediamine were used for the synthesis of product **5b**.

Beige powder; yield 2.39 g (82%); mp 111−112 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.72 (s, 1H), 8.15−8.09 (m, 2H), 7.98 (d, J = 5.3 Hz, 1H), 7.93−7.88 (m, 2H), 7.36 (d, J = 5.3 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 146.3, 142.7, 141.3, 140.7, 135.8, 132.8, 131.3, 131.1, 130.4, 128.9, 128.8, 109.8. Anal. Calcd for $C_{12}H_7BrN_2S$ (291.17): C, 49.50; H, 2.42; N, 9.62. Found: C, 49.54; H, 2.56; N, 9.38.

*2-(2-Bromophenyl)pyrazine (**5c**).* Commercially available material **5c** was used in our experiments.

*2-(2-Bromophenyl)quinoxaline (**5d**).* 2′-Bromoacetophenone and 1,2-phenylenediamine were used for the synthesis of product **5b**.

Pale yellow powder; yield 2.28 g (77%); mp 112−113 °C (ref 18 116−118 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.20 (s, 1H), 8.21 (td, J = 6.1, 3.2 Hz, 2H), 7.85 (dt, J = 6.4, 3.4 Hz, 2H), 7.76 (dd, J = 8.0, 1.2 Hz, 1H), 7.69 (dd, J = 7.7, 1.8 Hz, 1H), 7.52 (td, J = 7.5, 1.2 Hz, 1H), 7.39 (td, J = 7.7, 1.7 Hz, 1H). Anal. Calcd for $C_{14}H_9BrN_2$ (285.14): C, 58.97; H, 3.18; N, 9.82. Found: C, 58.88; H, 3.38; N, 9.69. Data similar to the literature.[18]

General Procedure for the Synthesis of 5-Aryl-5*H*-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-*b*]indoles (3a−j). A stirred mixture of 5-(2-bromophenyl)-[1,2,5]oxadiazolo-[3,4-*b*]pyrazine (**1**) (135 mg, 0.5 mmol), corresponding anilines (0.6 mmol), tricyclohexylphosphine (28 mg, 20 mol %), $Pd(OAc)_2$ (11 mg, 10 mol %), and K_3PO_4 (265 mg, 1.25 mmol) in degassed 1,4-dioxane (15 mL) was heated at reflux under nitrogen for 15 h in a Schlenk tube. The reaction mixture was cooled, filtered, acidified with concentrated CH_3COOH (1 mL), and dissolved with a mixture of EtOAc and water 1:1 (50 mL), and the organic layer was separated. The aqueous layer was extracted with EtOAc (2 × 25 mL). The combined organic extracts were dried with $MgSO_4$ and the solvents were evaporated. The organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by column chromatography using hexane and ethyl acetate as an eluent.

*5-Phenyl-5H-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-b]-indole (**3a**).* Red powder; yield 65 mg (45%); mp 285−286

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°C. R_f 0.45 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.41−8.38 (m, 1H), 7.83 (ddd, J = 8.4, 7.5, 1.3 Hz, 1H), 7.72−7.70 (m, 4H), 7.62 (ddt, J = 6.5, 4.9, 3.3 Hz, 1H), 7.50 (td, J = 7.6, 0.8 Hz, 1H), 7.32 (d, J = 8.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6): δ 153.2, 151.7, 151.5, 148.8, 135.8, 133.5, 130.0, 129.0, 127.1, 124.8, 123.6, 118.3, 111.4. IR (DRA): 434, 446, 466, 496, 565, 592, 617, 627, 666, 691, 749, 775, 796, 807, 857, 880, 915, 946, 1008, 1019, 1030, 1057, 1081, 1110, 1168, 1180, 1128, 1259, 1307, 1330, 1379, 1445, 1486, 1502, 1551, 1586, 1598, 1621, 3079, 3099 cm^{-1}. Anal. Calcd for $C_{16}H_9N_5O$ (287.28): C, 66.89; H, 3.16; N, 24.38. Found: C, 66.81; H, 3.18; N, 24.35.

*5-(2-Methoxyphenyl)-5H-[1,2,5]oxadiazolo[3′,4′:5,6]-pyrazino[2,3-b]indole (**3b**).* Red powder; yield 22 mg (14%); mp 248−250 °C. R_f 0.31 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.38 (dd, J = 7.7, 1.2 Hz, 1H), 7.80 (ddd, J = 8.4, 7.4, 1.3 Hz, 1H), 7.67−7.63 (m, 1H), 7.61 (dd, J = 7.7, 1.7 Hz, 1H), 7.48 (td, J = 7.5, 0.9 Hz, 1H), 7.41 (dd, J = 8.5, 1.2 Hz, 1H), 7.25 (td, J = 7.6, 1.2 Hz, 1H), 7.05 (d, J = 8.1 Hz, 1H), 3.77 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 155.7, 153.3, 152.2, 152.1, 149.5, 136.4, 131.8, 130.2, 125.1, 123.9, 121.7, 118.5, 113.7, 112.5, 56.3. Anal. Calcd for $C_{17}H_{11}N_5O_2$ (317.30): C, 64.35; H, 3.49; N, 22.07. Found: C, 64.42; H, 3.45; N, 21.93.

*5-(3-Methoxyphenyl)-5H-[1,2,5]oxadiazolo[3′,4′:5,6]-pyrazino[2,3-b]indole (**3c**).* Red powder; yield 76 mg (48%); mp 258−260 °C. R_f 0.25 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.42−8.37 (m, 1H), 7.83 (ddd, J = 8.4, 7.4, 1.3 Hz, 1H), 7.63 (t, J = 8.3 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.36 (d, J = 8.2 Hz, 1H), 7.28 (dt, J = 3.6, 1.4 Hz, 2H), 7.21 (ddd, J = 8.4, 2.5, 1.0 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 153.7, 152.2, 152.1, 152.0, 149.3, 136.4, 135.0, 131.3, 125.3, 124.1, 119.7, 118.8, 115.2, 113.4, 112.1, 56.0. Anal. Calcd for $C_{17}H_{11}N_5O_2$ (317.30): C, 64.35; H, 3.49; N, 22.07. Found: C, 64.30; H, 3.58; N, 22.09.

*5-(4-Methoxyphenyl)-5H-[1,2,5]oxadiazolo[3′,4′:5,6]-pyrazino[2,3-b]indole (**3d**).* Orange powder; yield 95 mg (60%); mp 271−273 °C. R_f 0.18 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.37 (ddd, J = 7.7, 1.3, 0.6 Hz, 1H), 7.81 (ddd, J = 8.5, 7.4, 1.3 Hz, 1H), 7.63−7.59 (m, 2H), 7.48 (td, J = 7.6, 0.8 Hz, 1H), 7.27−7.23 (m, 3H), 3.89 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 159.4, 153.2, 151.7, 151.5, 149.2, 135.8, 128.6, 125.9, 124.7, 123.4, 118.2, 115.2, 111.4, 55.5. IR (DRA): 453, 464, 484, 529, 567, 592, 623, 635, 644, 694, 725, 755, 771, 788, 797, 804, 815, 835, 842, 852, 875, 911, 936, 953, 969, 987, 1007, 1015, 1028, 1058, 1111, 1155, 1180, 1232, 1263, 1304, 1326, 1384, 1445, 1465, 1488, 1518, 1552, 1595, 1610, 1619, 3009, 3062 cm^{-1}. Anal. Calcd for $C_{17}H_{11}N_5O_2$ (317.30): C, 64.35; H, 3.49; N, 22.07. Found: C, 64.51; H, 3.54; N, 22.26.

*5-(3,4-Dimethoxyphenyl)-5H-[1,2,5]oxadiazolo[3′,4′:5,6]-pyrazino[2,3-b]indole (**3e**).* Red powder; yield 111 mg (64%); mp 271−272 °C. R_f 0.28 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.37 (dt, J = 7.7, 0.9 Hz, 1H), 7.81 (ddd, J = 8.4, 7.4, 1.3 Hz, 1H), 7.48 (td, J = 7.5, 0.8 Hz, 1H), 7.30 (d, J = 8.1 Hz, 1H), 7.26 (dd, J = 5.4, 3.2 Hz, 2H), 7.22 (dd, J = 8.5, 2.2 Hz, 1H), 3.89 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 153.2, 151.8, 151.5, 149.5, 149.4, 149.2, 135.8, 125.9, 124.6, 123.4, 119.8, 118.1, 112.3, 111.6, 110.9, 55.8. Anal. Calcd for $C_{18}H_{13}N_5O_3$ (347.33): C, 62.24; H, 3.77; N, 20.16. Found: C, 62.12; H, 3.61; N, 20.08.

*5-(2-Nitrophenyl)-5H-[1,2,5]oxadiazolo[3′,4′:5,6]-pyrazino[2,3-b]indole (**3f**).* Orange powder; yield 17 mg (10%); mp 274−275 °C. R_f 0.45 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.51−8.36 (m, 2H), 8.12 (td, J = 7.7, 1.5 Hz, 1H), 7.98 (ddd, J = 8.3, 6.5, 1.6 Hz, 2H), 7.89−7.83 (m, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.29 (d, J = 8.2 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 153.1, 152.1, 151.9, 151.8, 148.8, 146.4, 136.7, 136.4, 132.0, 131.6, 127.0, 126.9, 125.5, 124.7, 118.8, 112.1. Anal. Calcd for $C_{16}H_8N_6O_3$ (332.27): C, 57.84; H, 2.43; N, 25.29. Found: C, 57.89; H, 2.34; N, 25.17.

*5-(3-Nitrophenyl)-5H-[1,2,5]oxadiazolo[3′,4′:5,6]-pyrazino[2,3-b]indole (**3g**).* Orange powder; yield 56 mg (34%); mp 287−290 °C (decomp.). R_f 0.36 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.60 (t, J = 2.2 Hz, 1H), 8.48 (ddd, J = 8.3, 2.3, 1.0 Hz, 1H), 8.43 (dd, J = 7.7, 1.2 Hz, 1H), 8.23 (ddd, J = 7.9, 2.1, 1.0 Hz, 1H), 8.03 (t, J = 8.1 Hz, 1H), 7.86 (ddd, J = 8.5, 7.4, 1.3 Hz, 1H), 7.54 (td, J = 7.5, 0.8 Hz, 1H), 7.47 (d, J = 8.2 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 153.7, 152.2, 152.1, 152.0, 149.1, 148.7, 136.4, 135.0, 134.3, 132.1, 125.4, 124.5, 124.3, 122.9, 119.0, 112.0. Anal. Calcd for $C_{16}H_8N_6O_3$ (332.27): C, 57.84; H, 2.43; N, 25.29. Found: C, 57.80; H, 2.25; N, 25.18.

*5-(4-Nitrophenyl)-5H-[1,2,5]oxadiazolo[3′,4′:5,6]-pyrazino[2,3-b]indole (**3h**).* Orange powder; yield 91 mg (55%); mp 271−273 °C. R_f 0.35 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.60−8.56 (m, 2H), 8.44 (dd, J = 7.8, 1.2 Hz, 1H), 8.09−8.05 (m, 2H), 7.88 (ddd, J = 8.5, 7.4, 1.3 Hz, 1H), 7.57−7.52 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 153.8, 152.2, 152.1, 152.0, 148.2, 147.2, 139.7, 136.4, 128.5, 125.8, 125.5, 124.7, 119.2, 112.2. IR (DRA): 463, 477, 492, 529, 598, 623, 689, 709, 747, 770, 793, 804, 827, 853, 865, 885, 913, 944, 1012, 1025, 1044, 1061, 1109, 1159, 1174, 1228, 1296, 1324, 1353, 1377, 1421, 1446, 1464, 1487, 1504, 1524, 1552, 1590, 1614, 3077, 3118 cm^{-1}. Anal. Calcd for $C_{16}H_8N_6O_3$ (332.27): C, 57.84; H, 2.43; N, 25.29. Found: C, 57.54; H, 2.42; N, 25.15.

*5-(m-Tolyl)-5H-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-b]indole (**3i**).* Red powder; yield 93 mg (62%); mp 262−264 °C. R_f 0.47 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.38 (d, J = 7.6 Hz, 1H), 7.87−7.77 (m, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.52−7.46 (m, 3H), 7.43 (d, J = 7.6 Hz, 1H), 7.31 (d, J = 8.2 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ 153.2, 151.7, 151.5, 148.8, 139.6, 135.8, 133.4, 129.8, 129.7, 127.4, 124.7, 124.2, 123.5, 118.3, 111.5, 20.9. Anal. Calcd for $C_{17}H_{11}N_5O$ (301.30): C, 67.77; H, 3.68; N, 23.24. Found: C, 67.88; H, 3.65; N, 23.41.

*5-Benzyl-5H-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-b]-indole (**3j**).* Red powder; yield 89 mg (59%); mp 210−212 °C. R_f 0.17 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.35−8.30 (m, 1H), 7.81 (td, J = 7.8, 7.4, 1.3 Hz, 1H), 7.57 (d, J = 8.2 Hz, 1H), 7.50−7.44 (m, 2H), 7.42 (t, J = 7.5 Hz, 1H), 7.34 (dd, J = 8.2, 6.6 Hz, 2H), 7.31−7.27 (m, 1H), 5.55 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 153.6, 152.3, 152.3, 151.9, 148.5, 136.1, 136.0, 129.2, 128.2, 128.0, 125.2, 123.6, 118.8, 112.2, 44.9. Anal. Calcd for $C_{17}H_{11}N_5O$ (301.30): C, 67.77; H, 3.68; N, 23.24. Found: C, 67.56; H, 3.81; N, 23.24.

General Procedure for the Synthesis of *N*-Aryl-6-(2-bromophenyl)-[1,2,5]oxadiazolo[3,4-*b*]pyrazin-5-amines (4a−i). A stirred mixture of 5-(2-bromophenyl)-[1,2,5]oxadiazolo[3,4-*b*]pyrazine (**1**) (135 mg, 0.5 mmol), corresponding anilines (0.6 mmol), and sodium hydride (24 mg, 1.0 mmol) in dry 1,4-dioxane (5 mL) was stirred at room temperature for 48 h. The reaction mixture was acidified with

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concentrated CH_3COOH (1 mL). The solvent was distilled off *in vacuo*, and the crude product was purified by column chromatography using hexane and ethyl acetate as an eluent.

*6-(2-Bromophenyl)-N-phenyl-[1,2,5]oxadiazolo[3,4-b]-pyrazin-5-amine (**4a**).* Yellow powder; yield 65 mg (55%); mp 174−175 °C. R_f 0.26 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 9.43 (s, 1H), 7.85 (dd, J = 8.1, 1.1 Hz, 1H), 7.76 (dd, J = 7.6, 1.7 Hz, 1H), 7.67 (td, J = 7.6, 1.2 Hz, 1H), 7.63−7.57 (m, 3H), 7.46−7.40 (m, 2H), 7.26 (tt, J = 7.3, 1.2 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.4, 152.4, 152.3, 150.2, 137.8, 133.5, 132.9, 132.0, 130.5, 129.0, 128.9, 127.6, 126.4, 124.8, 121.7. Anal. Calcd for $C_{16}H_{10}BrN_5O$ (368.19): C, 52.19; H, 2.74; N, 19.02. Found: C, 52.37; H, 2.63; N, 18.97.

*6-(2-Bromophenyl)-N-(2-methoxyphenyl)-[1,2,5]-oxadiazolo[3,4-b]pyrazin-5-amine (**4b**).* Orange powder; yield 108 mg (54%); mp 207−208 °C. R_f 0.42 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.43 (s, 1H), 8.35−8.28 (m, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.82 (dd, J = 7.5, 1.7 Hz, 1H), 7.75 (t, J = 7.5 Hz, 1H), 7.68 (td, J = 7.8, 1.7 Hz, 1H), 7.27−7.20 (m, 1H), 7.14−7.06 (m, 2H), 3.68 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.2, 152.4, 151.2, 150.4, 150.1, 134.8, 133.7, 133.4, 131.6, 129.3, 126.8, 126.7, 122.0, 121.5, 121.3, 111.9, 56.7. Anal. Calcd for $C_{17}H_{12}BrN_5O_2$ (398.21): C, 51.27; H, 3.04; N, 17.59. Found: C, 51.50; H, 3.12; N, 17.81.

*6-(2-Bromophenyl)-N-(3-methoxyphenyl)-[1,2,5]-oxadiazolo[3,4-b]pyrazin-5-amine (**4c**).* Yellow powder; yield 115 mg (58%); mp 171−172 °C. R_f 0.32 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 9.36 (s, 1H), 7.85 (dd, J = 8.1, 1.1 Hz, 1H), 7.75 (dd, J = 7.6, 1.7 Hz, 1H), 7.66 (td, J = 7.6, 1.2 Hz, 1H), 7.59 (ddd, J = 8.2, 7.4, 1.7 Hz, 1H), 7.34 (t, J = 8.1 Hz, 1H), 7.27−7.19 (m, 2H), 6.85 (ddd, J = 8.3, 2.6, 1.0 Hz, 1H), 3.76 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.3, 159.7, 152.3, 152.2, 150.2, 139.0, 135.8, 133.5, 132.9, 132.1, 129.8, 128.9, 121.8, 117.0, 111.6, 110.6, 55.7. Anal. Calcd for $C_{17}H_{12}BrN_5O_2$ (398.21): C, 51.27; H, 3.04; N, 17.59. Found: C, 51.40; H, 2.97; N, 17.32.

*6-(2-Bromophenyl)-N-(4-methoxyphenyl)-[1,2,5]-oxadiazolo[3,4-b]pyrazin-5-amine (**4d**).* Red powder; yield 125 mg (63%); mp 117−119 °C. R_f 0.35 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.34 (s, 1H), 7.84 (dd, J = 8.0, 1.1 Hz, 1H), 7.74 (dd, J = 7.6, 1.7 Hz, 1H), 7.65 (td, J = 7.5, 1.1 Hz, 1H), 7.58 (td, J = 7.8, 1.8 Hz, 1H), 7.53−7.45 (m, 2H), 7.02−6.97 (m, 2H), 3.77 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.5, 157.7, 152.5, 152.4, 150.2, 135.9, 133.5, 132.9, 131.9, 130.6, 128.9, 126.4, 121.7, 114.2, 55.8. Anal. Calcd for $C_{17}H_{12}BrN_5O_2$ (398.21): C, 51.27; H, 3.04; N, 17.59. Found: C, 51.50; H, 3.21; N, 17.58.

*6-(2-Bromophenyl)-N-(3,4-dimethoxyphenyl)-[1,2,5]-oxadiazolo[3,4-b]pyrazin-5-amine (**4e**).* Dark red powder; yield 109 mg (51%); mp 166−167 °C. R_f 0.20 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 9.29 (s, 1H), 7.97−7.84 (m, 1H), 7.75 (dd, J = 7.6, 1.8 Hz, 1H), 7.66 (td, J = 7.6, 1.1 Hz, 1H), 7.59 (td, J = 7.8, 1.8 Hz, 1H), 7.29−7.22 (m, 1H), 7.15 (d, J = 2.4 Hz, 1H), 7.01 (d, J = 8.7 Hz, 1H), 3.78 (s, 3H), 3.73 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.4, 152.5, 152.3, 150.2, 148.7, 147.4, 135.8, 133.5, 132.9, 131.9, 130.8, 128.9, 121.7, 117.2, 111.9, 109.3, 56.13, 56.11. Anal. Calcd for $C_{18}H_{14}BrN_5O_3$ (428.24): C, 50.48; H, 3.30; N, 16.35. Found: C, 50.57; H, 3.28; N, 16.07.

*6-(2-Bromophenyl)-N-(3-nitrophenyl)-[1,2,5]oxadiazolo-[3,4-b]pyrazin-5-amine (**4g**).* Dark orange powder; yield 52 mg (25%); mp 163−165 °C. R_f 0.15 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 9.75 (s, 1H), 8.58 (t, J = 2.2 Hz, 1H), 8.23 (ddd, J = 8.2, 2.1, 0.9 Hz, 1H), 8.10 (ddd, J = 8.2, 2.3, 0.9 Hz, 1H), 7.88 (dd, J = 8.1, 1.1 Hz, 1H), 7.78 (dd, J = 7.6, 1.7 Hz, 1H), 7.74 (t, J = 8.2 Hz, 1H), 7.69 (td, J = 7.5, 1.1 Hz, 1H), 7.63 (td, J = 7.8, 1.8 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.0, 152.2, 151.9, 150.3, 148.2, 139.2, 135.6, 133.6, 133.1, 132.2, 130.4, 130.4, 128.9, 121.8, 120.6, 118.7. Anal. Calcd for $C_{16}H_9BrN_6O_3$ (413.19): C, 46.51; H, 2.20; N, 20.34. Found: C, 46.36; H, 2.19; N, 20.07.

*6-(2-Bromophenyl)-N-(4-nitrophenyl)-[1,2,5]oxadiazolo-[3,4-b]pyrazin-5-amine (**4h**).* Orange powder; yield 79 mg (38%); mp 200−202 °C. R_f 0.23 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 9.81 (s, 1H), 8.36−8.29 (m, 2H), 8.06−8.01 (m, 2H), 7.87 (dd, J = 8.1, 1.1 Hz, 1H), 7.78 (dd, J = 7.6, 1.7 Hz, 1H), 7.69 (td, J = 7.5, 1.1 Hz, 1H), 7.62 (td, J = 7.8, 1.8 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.0, 151.9, 151.8, 150.3, 144.3, 144.2, 135.6, 133.6, 133.1, 132.4, 128.9, 124.8, 123.9, 121.8. Anal. Calcd for $C_{16}H_9BrN_6O_3$ (413.19): C, 46.51; H, 2.20; N, 20.34. Found: C, 46.71; H, 2.09; N, 20.36.

*6-(2-Bromophenyl)-N-(m-tolyl)-[1,2,5]oxadiazolo[3,4-b]-pyrazin-5-amine (**4i**).* Yellow powder; yield 102 mg (51%); mp 169−170 °C. R_f 0.50 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.35 (s, 1H), 7.85 (dd, J = 8.1, 1.1 Hz, 1H), 7.75 (dd, J = 7.6, 1.8 Hz, 1H), 7.66 (td, J = 7.5, 1.1 Hz, 1H), 7.58 (td, J = 7.8, 1.8 Hz, 1H), 7.50−7.44 (m, 1H), 7.37 (d, J = 2.0 Hz, 1H), 7.31 (t, J = 7.8 Hz, 1H), 7.07 (ddt, J = 7.5, 1.8, 0.9 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 160.9, 151.9, 151.8, 149.7, 137.8, 137.2, 135.3, 133.0, 132.4, 131.5, 128.4, 128.3, 126.6, 124.7, 121.4, 121.2, 21.0. Anal. Calcd for $C_{17}H_{12}BrN_5O_2$ (398.21): C, 51.27; H, 3.04; N, 17.59. Found: C, 51.37; H, 3.25; N, 17.54.

General Procedure for the Buchwald−Hartwig Cross-Coupling Reaction for the Synthesis of Compounds 6a and 7a. A stirred mixture of 5-(3-bromothiophen-2-yl)-[1,2,5]oxadiazolo[3,4-*b*]pyrazine (**5a**) (142 mg, 0.5 mmol), aniline (**2a**) (55 mg, 0.6 mmol), 4,5-*bis*(diphenylphosphino)-9,9-dimethylxanthene (Xantphos) (58 mg, 20 mol %), $Pd(OAc)_2$ (11 mg, 10 mol %), and K_3PO_4 (265 mg, 1.25 mmol) in degassed 1,4-dioxane (15 mL) was heated at reflux under nitrogen for 15 h in a Schlenk tube. The reaction mixture was cooled, filtered, and dissolved with a mixture of AcOEt and water 1:1 (50 mL), and the organic layer was separated. The aqueous layer was extracted with AcOEt (2 × 25 mL). The combined organic extracts were dried with $MgSO_4$ and the solvents were evaporated. The organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated. The crude products **6a** and **7a** were purified by column chromatography using hexane and ethyl acetate as an eluent.

*2-([1,2,5]Oxadiazolo[3,4-b]pyrazin-5-yl)-N-phenylthiophen-3-amine (**6a**).* Violet powder; yield 15 mg (10%); mp 167−169 °C. R_f 0.12 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.83 (s, 1H), 9.19 (s, 1H), 8.18 (d, J = 5.5 Hz, 1H), 7.46−7.42 (m, 2H), 7.36−7.34 (m, 2H), 7.32 (d, J = 5.5 Hz, 1H), 7.18 (tt, J = 7.2, 1.2 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 157.2, 154.2, 152.1, 151.3, 150.7, 140.1, 137.4, 129.7, 124.1, 120.7, 118.7, 111.7. Anal. Calcd for $C_{14}H_9N_5OS$ (295.32): C, 56.94; H, 3.07; N, 23.71. Found: C, 56.72; H, 3.01; N, 23.48.

*8-Phenyl-8H-[1,2,5]oxadiazolo[3,4-b]thieno[2′,3′:4,5]-pyrrolo[2,3-e]pyrazine (**7a**).* Orange powder; yield 109 mg (74%); mp 274−275 °C. R_f 0.21 ($CHCl_3$/hexane = 1:1, v/v).

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^{1}H NMR (600 MHz, DMSO-d_6): δ 8.54 (d, J = 5.1 Hz, 1H), 7.80−7.77 (m, 2H), 7.70−7.67 (m, 2H), 7.55 (td, J = 7.3, 1.2 Hz, 1H), 7.42 (d, J = 5.1 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 159.4, 153.7, 151.6, 151.0, 148.0, 143.9, 135.1, 130.3, 128.7, 125.7, 114.6, 113.0. IR (DRA): 447, 485, 514, 556, 592, 606, 619, 649, 663, 675, 690, 704, 743, 759, 780, 793, 829, 859, 867, 882, 894, 915, 994, 1008, 1031, 1041, 1058, 1078, 1094, 1109, 1162, 1198, 1230, 1244, 1290, 1315, 1360, 1383, 1404, 1449, 1474, 1497, 1545, 1557, 1591, 3093, 3107 cm^{-1}. Anal. Calcd for $C_{14}H_7N_5OS$ (293.30): C, 57.33; H, 2.41; N, 23.88. Found: C, 57.50; H, 2.47; N, 23.99.

General Procedure for the Buchwald−Hartwig Cross-Coupling Reaction for the Synthesis of Compounds 6b, 6c, and 6d. A stirred mixture of *N*-phenyl-2-(quinoxalin-2-yl)thiophen-3-amine (**5b**) [*N*-phenyl-2-(pyrazin-2-yl)aniline (**5c**) or *N*-phenyl-2-(quinoxalin-2-yl)aniline (**5d**) (0.5 mmol), aniline (**2a**) (55 mg, 0.6 mmol), 4,5-*bis*(diphenylphosphino)-9,9-dimethylxanthene (Xantphos) (58 mg, 20 mol %), $Pd(OAc)_2$ (11 mg, 10 mol %), and K_3PO_4 (265 mg, 1.25 mmol) in degassed 1,4-dioxane (15 mL) was heated at reflux under nitrogen for 15 h in a Schlenk tube. The reaction mixture was cooled, filtered, and dissolved with a mixture of AcOEt and water 1:1 (50 mL), and the organic layer was separated. The aqueous layer was extracted with AcOEt (2 × 25 mL). The combined organic extracts were dried with $MgSO_4$ and the solvents were evaporated. The organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated. The crude products **6b−d** were purified by column chromatography using hexane and ethyl acetate as an eluent.

*N-Phenyl-2-(quinoxalin-2-yl)thiophen-3-amine (**6b**).* Orange powder; yield 135 mg (89%); mp 148−150 °C. R_f 0.41 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.38 (s, 1H), 9.11 (s, 1H), 8.10 (dd, J = 8.3, 1.3 Hz, 1H), 8.01 (dd, J = 8.2, 1.4 Hz, 1H), 7.85 (d, J = 5.4 Hz, 1H), 7.82 (ddd, J = 8.3, 6.9, 1.5 Hz, 1H), 7.72 (ddd, J = 8.3, 6.9, 1.4 Hz, 1H), 7.37−7.32 (m, 3H), 7.27−7.24 (m, 2H), 6.99 (tt, J = 7.3, 1.2 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 148.8, 145.5, 143.9, 142.4, 140.2, 139.3, 130.7, 130.1, 129.5, 128.7, 128.4, 127.8, 121.4, 120.8, 117.9, 113.5. Anal. Calcd for $C_{18}H_{13}N_3S$ (303.38): C, 71.26; H, 4.32; N, 13.85. Found: C, 71.07; H, 4.23; N, 13.84.

*N-Phenyl-2-(pyrazin-2-yl)aniline (**6c**).* Yellow powder; yield 98 mg (79%); mp 82−84 °C. R_f 0.37 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.22 (s, 1H), 9.07 (d, J = 1.5 Hz, 1H), 8.72 (t, J = 2.0 Hz, 1H), 8.57 (d, J = 2.6 Hz, 1H), 7.78 (d, J = 7.7 Hz, 1H), 7.38 (d, J = 4.0 Hz, 2H), 7.22 (t, J = 7.8 Hz, 2H), 7.10−7.02 (m, 3H), 6.86 (t, J = 7.3 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 153.1, 144.4, 142.9, 142.8, 142.1, 142.0, 130.5, 130.5, 129.2, 124.3, 120.8, 120.6, 118.5, 117.9. Anal. Calcd for $C_{16}H_{13}N_3$ (247.29): C, 77.71; H, 5.30; N, 16.99. Found: C, 77.72; H, 5.29; N, 17.02.

*N-Phenyl-2-(quinoxalin-2-yl)aniline (**6d**).* Yellow powder; yield 144 mg (77%); mp 122−123 °C. R_f 0.23 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.93 (s, 1H), 9.38 (s, 1H), 8.22 (dd, J = 8.2, 1.5 Hz, 1H), 8.09 (dd, J = 8.2, 1.5 Hz, 1H), 8.03 (dd, J = 7.9, 1.5 Hz, 1H), 7.87 (dddd, J = 22.6, 8.4, 7.0, 1.5 Hz, 2H), 7.49−7.42 (m, 2H), 7.27 (dd, J = 8.5, 7.2 Hz, 2H), 7.20−7.15 (m, 2H), 7.10 (ddd, J = 8.1, 7.0, 1.4 Hz, 1H), 6.90 (tt, J = 7.2, 1.2 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 152.7, 145.8, 142.7, 142.5, 140.2, 139.9, 131.1, 130.9, 130.5, 129.7, 129.3, 128.7, 128.6, 123.6, 120.9, 120.5, 118.1, 117.9. Anal. Calcd for $C_{20}H_{15}N_3$ (297.35): C, 80.78; H, 5.08; N, 14.13. Found: C, 80.70; H, 5.02; N, 14.20.

Synthesis of 4-Phenyl-4*H*-thieno[2′,3′:4,5]pyrrolo-[2,3-*b*]quinoxaline (7b). The suspension of *N*-phenyl-2-(quinoxalin-2-yl)thiophen-3-amine (**6b**) (152 mg, 0.5 mmol) in trifluoroacetic acid (5 mL) was stirred at 50 °C for 24 h. The solvent was removed under reduced pressure. The crude product **7b** was purified by column chromatography using hexane and ethyl acetate as an eluent.

*4-Phenyl-4H-thieno[2′,3′:4,5]pyrrolo[2,3-b]quinoxaline (**7b**).* Dark orange powder; yield 122 mg (81%); mp 200−201 °C. R_f 0.61 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.03 (d, J = 8.0 Hz, 1H), 7.85 (dd, J = 40.7, 8.1 Hz, 2H), 7.52 (dt, J = 21.7, 7.3 Hz, 2H), 7.31−7.21 (m, 2H), 7.07 (t, J = 7.5 Hz, 1H), 6.55 (dd, J = 62.2, 6.7 Hz, 2H), 5.96 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.1, 147.6, 147.2, 141.6, 141.4, 133.5, 131.2, 130.4, 129.7, 129.0, 128.4, 127.9, 126.7, 123.9, 121.7, 119.1. IR (DRA): 511, 538, 572, 607, 647, 698, 718, 737, 753, 789, 804, 841, 866, 894, 944, 974, 1017, 1048, 1062, 1100, 1128, 1139, 1164, 1190, 1209, 1234, 1272, 1313, 1348, 1380, 1402, 1430, 1446, 1482, 1516, 1529, 1577, 1596, 1618, 3057, 3099, 3181, 3279 cm^{-1}. Anal. Calcd for $C_{18}H_{11}N_3S$ (301.37): C, 71.74; H, 3.68; N, 13.94. Found: C, 71.86; H, 3.35; N, 14.07.

General Procedure for the Synthesis of 5-Phenyl-5*H*-pyrazino[2,3-*b*]indole (7c) and 6-Phenyl-6*H*-indolo[2,3-*b*]quinoxaline (7d). The suspension of *N*-phenyl-2-(pyrazin-2-yl)aniline (**6c**) [or *N*-phenyl-2-(quinoxalin-2-yl)aniline (**6d**)] (0.5 mmol) in EtOH/conc. HCl (10 mL, v/v 99:1) was refluxed for 1 h. The solvent was removed under reduced pressure. The crude products **7c** and **7d** were purified by column chromatography using hexane and ethyl acetate as an eluent.

*5-Phenyl-5H-pyrazino[2,3-b]indole (**7c**).* Beige powder; yield 98 mg (80%); mp 158−160 °C. R_f 0.52 (EtOAc/hexane = 1:2, v/v). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.56 (d, J = 2.7 Hz, 1H), 8.43 (dt, J = 7.8, 1.0 Hz, 1H), 8.40 (d, J = 2.7 Hz, 1H), 7.65−7.60 (m, 4H), 7.59 (dd, J = 7.0, 1.3 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.50 (tt, J = 5.8, 2.6 Hz, 1H), 7.44 (ddd, J = 8.0, 7.0, 1.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 145.8, 141.4, 139.8, 137.6, 136.6, 135.3, 129.8, 129.3, 128.1, 127.1, 121.8, 121.7, 119.9, 110.7. IR (DRA): 449, 492, 533, 569, 594, 619, 638, 655, 695, 715, 740, 748, 762, 794, 804, 845, 866, 906, 936, 951, 973, 1012, 1024, 1077, 1104, 1149, 1157, 1171, 1211, 1230, 1270, 1281, 1304, 1327, 1344, 1407, 1456, 1477, 1503, 1545, 1579, 1596, 1621, 3055, 3072 cm^{-1}. Anal. Calcd for $C_{16}H_{11}N_3$ (245.28): C, 78.35; H, 4.52; N, 17.13. Found: C, 78.34; H, 4.76; N, 17.16.

*6-Phenyl-6H-indolo[2,3-b]quinoxaline (**7d**).* Pale yellow powder; yield 109 mg (74%); mp 237−238 °C. R_f 0.32 ($CHCl_3$/hexane = 1:1, v/v). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.57−8.51 (m, 1H), 8.32 (dd, J = 7.9, 1.9 Hz, 1H), 8.09 (dd, J = 7.9, 1.9 Hz, 1H), 7.77−7.62 (m, 7H), 7.54−7.49 (m, 2H), 7.44 (t, J = 7.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 145.8, 144.7, 140.5, 140.1, 139.8, 135.4, 131.0, 129.8, 129.2, 128.8, 128.2, 127.9, 127.1, 126.5, 122.6, 121.8, 119.8, 110.6. IR (DRA): 591, 619, 650, 695, 720, 749, 767, 781, 802, 830, 859, 909, 924, 955, 1007, 1016, 1027, 1043, 1074, 1101, 1134, 1148, 1175, 1207, 1228, 1254, 1305, 1320, 1337, 1355, 1392, 1405, 1460, 1471, 1484, 1504, 1583, 1598, 1609, 1629, 3057 cm^{-1}. Anal. Calcd for $C_{20}H_{13}N_3$ (295.34): C, 81.34; H, 4.44; N, 14.23. Found: C, 81.30; H, 4.51; N, 14.21.

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■ ASSOCIATED CONTENT

Supporting Information

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Crystallographic data for **3i** (CIF)

Experimental procedures, UV−vis absorption spectra of compounds **3a**, **3d**, **3h**, and **7a−d**, characterization data for all new compounds, and ^{1}H and ^{13}C NMR spectra (PDF)

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Notes

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